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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,756	10/02/2003	Mary Jo Ondrechen	NU-593XX	6620

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EXAMINER	
RIGGS II, LARRY D	
ART UNIT	**PAPER NUMBER**
1631	
MAIL DATE	**DELIVERY MODE**
12/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/678,756	**Applicant(s)** ONDRECHEN ET AL.	
	Examiner LARRY D. RIGGS II	**Art Unit** 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _15 August 2008_.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-17_ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _1-17_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed 15 August 2008 are acknowledged and entered.

Status of Claims

Claims 1-17 are currently pending and under consideration.

Withdrawn Rejections/Objections

The rejection of claims 1-17 under 35 U.S.C. 112, Second Paragraph, in the Office action mailed 20 May 2008 is withdrawn in view of the amendments filed 15 August 2008.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The recent en banc decision regarding Bilski v. Warsaw (2008) set forth that a process is patent-eligible if (1) it is ties to a particular machine or apparatus or (2) it transforms a particular article into a different state or thing.

The instant claims are drawn to a method for determining interaction sites in a protein having an identified three-dimensional structure. The instant claims are drawn the abstract process steps of providing an identified 3D protein structure, identifying ionizable amino acid residues having anomalous titration curve behavior, clustering certain identified ionizable amino acid residues into putative interaction sites and displaying said putative interaction sites.

The instant claims do not recite or inherently involve any transformation of an article, therefore the Examiner must determine if the instant claims have a tie to a particular machine or apparatus. Instant claims 1-17 do not recite any limitation that ties the recited abstract process to any particular machine or apparatus.

Further, displaying said interval scores is an insignificant post-solution activity. Nominal or token recitations will not suffice, E.g. displaying, inputting, obtaining, See Ex parte Langemyr (May 28, 2008). Applicants are cautioned against introduction of new matter in an amendment.

For these reasons, claims 1-20 are considered non-statutory subject matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Beroza et al, (Biophysical Journal, 1995, 68, 2233-2250).

The instant claim 1 provides a method for determining interaction sites in a protein having an identified three-dimensional structure, comprising: providing an identified three-dimensional structure for said protein, identifying in said structure, ionizable amino acid residues having anomalous predicted theoretical microscopic titration curve behavior, clustering certain of said identified ionizable amino acid residues into putative interaction sites, and displaying said interaction sites determination.

Regarding claim 1, Beroza et al. shows an identified three dimensional structure of reaction center (RC) protein from *Rb. sphaeroides*, (page 2234, left column, first paragraph), identified ionizable amino acid residues Glu L212, Asp L210, Asp L213, etc., with anomalous predicted titration curves, (page 2248, left column, second paragraph; Figure 3), clustering of ionizable amino acid residues with anomalous curves into putative interaction sites and displayed, (page 2248, left column, first and second paragraphs; page 2248, right column, last paragraph – page 2249, left column; Tables 2-6, Figure 3).

Regarding claim 2, Beroza et al. shows calculating an electrical potential function for the RC structure, (2234, left column, third paragraph), calculating titration curves for ionizable amino acid residues, (2234, right column, second paragraph – 2236, right column, first paragraph; Tables 2 and 3), evaluating shapes of amino acid residue titration curves and distinguishing anomalous titration curves, (2248, left column, second paragraph; Figure 3), clustering of ionizable amino acid residues with anomalous curves into putative interaction sites and displayed, (page 2248, left column, first and second paragraphs; page 2248, right column, last paragraph – page 2249, left column; Tables 2-6, Figure 3).

Regarding claim 3, Beroza et al. shows Asp L213 is probably an artifact of the computational model and may not be considered part of the cluster with Glu L212 and Asp L210, (2242, right column, third paragraph).

Regarding claim 5, Beroza et al. shows the crystallographic three dimensional structure of reaction center (RC) protein from *Rb. sphaeroides* determined from , (page 2234, left column, first paragraph).

Regarding claim 11, Beroza et al. shows elongated titration curve over a wide pH range, (Abstract, 2242, left column, last paragraph; Figure 3).

Regarding claim 12, Beroza et al. shows anomalous titrations visually, (Figure 3).

Regarding claim 13, Beroza et al. shows titration of residues that are near the quinine binding sites, (2234, left column, second paragraph; Figure 1).

Declaration under 37 C.F.R. 1.132

The declarations of Mary Jo Ondrechen, filed 15 August 2008 have been considered.

The declarations of Mary Jo Ondrechen, filed 15 August 2008 under 37 CFR 1.132 is insufficient to overcome the rejection of claims 1-3, 5 and 11-13 under 35 U.S.C. 102(b) as being anticipated by Beroza et al, (Biophysical Journal, 1995, 68, 2233-2250) as set forth in the last Office action. The declarations of Mary Jo Ondrechen form only a statement of opinion regarding the general subject matter of the instant application and that of the applied prior art. The opinion statements do not sufficiently identify and differentiate that which is expressly recited in the instant claims from that which is taught in the prior art. The opinion statement amounts to a general conclusion that the instant claims are free of the art and is therefore not persuasive against the prior art rejections of record.

Response to Arguments

Applicant's arguments filed 15 August 2008 have been fully considered but they are not persuasive.

Applicant's argues Beroza starts with reactive sites, Qa and Qb, and then identifies residues of interest around the quinones using displayed information, not the other way around like the instant invention. Applicants argue that while there may be three perturbed theoretical titration curves near Qb there is only one such residue near Qa, which doesn't suffice as a cluster and meet the limitations of claim 1. Applicants argue that there is nothing to indicate the "phenomenon" in Beroza et al. could be general and allow one skilled in the art to identify reactive areas inside a protein. Applicants argue that no limitations of claim 2 are suggested by the Examiner as being taught by Beroza et al. Applicants argue that Beroza et al. eliminates an amino acid from a cluster that does not fit instead of teaching claim 3. Applicants argue that deficiencies in Beroza et al. do not make up for what is taught regarding claims 5, and 11-13.

Applicant's arguments are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. putative interactive sites from clusters of anomalous titration curve behavior of amino acids) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Beroza et al. shows numerous large clusters of interacting sites of the RC protein, wherein only a few amino acids are identified to be putative interaction sites, i.e. influence on electron transfer, from the clustering of anomalous titrations of amino acids, (pages 2234, left column, 2236, right column, 2239, 2240, right column; Tables 2-3). Beroza et al. shows clusters of amino acids with anomalous titration curves, (page 2246; Figure 3), whether groups of amino acids with anomalous titration curves are in particular areas, i.e. Qa or Qb, of the RC protein is not a limitation of the instant claims. Beroza et al. does not discover a phenomenon but identifies anomalous titrations of amino acids that indicate amino acids with the greatest influence on electron transfer, i.e. putative interaction sites, (page 2248, left column). Regarding claim 2, Beroza et al.

shows titration of each ionizable amino acid in the RC protein, (page 2234, left column, first paragraph; page 2234, right column - 2235, right column). Beroza et al. shows evaluating shapes of amino acid titration curves to discover anomalous titration curves, (page 2248, left column, first full paragraph). Regarding claim 3, Beroza identifies a a perturbed titration curve residue that falls outside a cluster, (2242, right column, third paragraph), eliminating "valid data for a residue that does not fit a theory" is not a limitation of claim 3. Beroza et al. meets all limitations of claims 1-3, 5 and 11-13 and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beroza et al, (Biophysical Journal, 1995, 68, 2233-2250), as applied to claims 1-3, 5 and 11-13 above, in view of Guex et al., (Electrophoresis, 1997, 18, 2714-2723).

Beroza et al. is applied to claims 1-3, 5 and 11-13 above.

Beroza et al. does not show a three dimensional protein structure downloaded from a database.

Regarding claim 4, Guex et al. shows three dimensional downloadable protein structure models, (2714, right column, first paragraph; 2718, left column, last paragraph – right column, second paragraph; Figures 1, 3-5).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the analysis of interaction site amino acids of Beroza et al. with the downloadable three dimensional protein structures by Guex et al. wherein the motivation would have been to access the numerous available proteins in protein databases, (Guex, 2714, left column, first paragraph).

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beroza et al, (Biophysical Journal, 1995, 68, 2233-2250), as applied to claims 1-3, 5 and 11-13 above, in view of Baker et al., (Science, 2001, 294, 93-96).

Beroza et al. is applied to claims 1-3, 5 and 11-13 above.

Beroza et al. does not show a three dimensional protein structure determined by comparative/homology modeling.

Regarding claim 17, Baker et al. shows three dimensional protein structure comparative modeling, (page 94, right column, last paragraph – page 95, right column, first paragraph; Figures 1-2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the analysis of interaction site amino acids of Beroza et al. with the comparative modeling of three dimensional protein structures by Baker et al. wherein the motivation would have been to utilize comparative modeling because with areas of research, such as structural genomics, the structure of most proteins will be modeled, (Baker et al., page 95, middle column, first paragraph).

Response to Arguments

Applicant's arguments filed 15 August 2008 have been fully considered but they are not persuasive.

Applicant's argues the combination of Beroza et al. Guex et al. or Baker et al. do not overcome deficiencies of Beroza et al.

Applicant's arguments are not persuasive because Beroza et al. does not have any deficiencies.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S DeJong/
Examiner, Art Unit 1631

/LDR/
Larry D. Riggs II
Examiner, Art Unit 1631